PRN 94-5: Requests for Re-considerations of Carcinogenicity Peer Review Decisions Based on Changes in Pathology Diagnoses

August 24, 1994

Attention: Persons Responsible For Registration of Pesticide Products

Subject: Requests for Re-considerations of Carcinogenicity Peer Review Decisions Based on Changes in Pathology Diagnoses.

This notice sets forth a procedure to be followed for submission of pathology re-reads to the Agency.

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I. Background

From time to time the Office of Pesticide Programs receives requests for re-consideration of Peer Review decisions based on re-evaluations of the pathology readings. These re-evaluations reflect voluntary activity on the part of the registrants, and are not the result of a requirement imposed by the Agency. The Agency is then asked to disregard the original readings and base its evaluation on the most recent ones. As a result the Agency may have two (or at times even more) pathological diagnoses for the same study.

Since this situation is occurring more and more frequently, the Agency is instituting a procedural requirement for any voluntary submissions of revised pathology diagnoses. This procedure will require a comprehensive peer review process, similar to the one used by the National Toxicology Program (NTP).

The National Toxicology Program (NTP) has a protocol for quality assurance in pathology, involving a quality assessment (peer review) pathologist and a Pathology Working Group (PWG) which is used to resolve differences in diagnoses between the laboratory (study) pathologist and the peer review pathologist. The PWG consists of a chair, the peer review pathologist and other pathologists (to include the study pathologist), all of whom are experienced in rodent toxicologic pathology. This group examines the tissues without knowledge of dose groups or previously rendered diagnoses. When the PWG consensus differs from the opinion of the study pathologist, the diagnosis is changed. Thus, the final diagnoses represent a consensus of study, peer review, and consultant pathologists on the PWG. This procedure is described in the NTP Technical Reports under the section: "Clinical Examinations and Pathology." EPA believes that the use of a PWG, similar to one used by NTP, should be part of every pathology re-evaluation.

II. Policy And Rationale

The Agency believes that a procedure for obtaining consensus in pathology re-reads will improve the quality of decision-making in classifying pesticide chemicals having carcinogenic potential. The

Agency has determined that unless the re-reads have been conducted using a Peer Review procedure, the Agency will base its evaluations upon the original readings.

The following will be required:

For any target tissue which is being re-evaluated, all slides containing that tissue in all dose groups, as well as the controls, must be re-read by the peer review pathologist. This is to include slides previously classified by the study pathologist as within normal limits, in addition to those having tumors, hyperplasia, hypertrophy, foci of cellular alteration or other non-neoplastic lesions.

The pathology reports from both the study and peer review pathologist and the original slides are to be submitted to a Pathology Working Group (PWG) similar to that described in the NTP Technical Reports under the section: "Clinical Examinations and Pathology." The PWG will review, as a minimum, all slides about which there were significantly differing diagnoses between the study and peer review pathologists.

Finally, the Agency should be provided with a detailed pathology report, which presents the PWG findings and includes the original diagnosis and the new diagnosis for each slide read, and a comment column to note any discrepancies, missing slides, etc.

The Agency also is considering including the requirement for review by a PWG for all original submissions in the future. This present Notice deals only with re-reads.

III. Effective Date

This policy notice is effective immediately. If you have questions, contact the Health Effects Division.

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Contact Us to ask a question, provide feedback, or report a problem.